

REMARKS

I. Preliminary Comments

The undersigned wishes to thank Examiners Schmidt and LeGuyader for allowing him the opportunity to discuss the outstanding office action with them on November 21, 2002. The substance of that discussion is included within this Response.

Claims 1, 4, 11, 12, 14-15, 17, 21, 22, 25, and 26 have been amended as set out above in order to more clearly present the subject matter of the invention. Attached hereto as Appendix A is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned **"VERSION WITH MARKINGS TO SHOW CHANGES MADE."** Also attached as Appendix B is a copy of all claims pending in the present application as amended.

Claims 1, 11, 14-15, 17, and 21 have been amended to include "variable number tandem repeat," which is the spelled out meaning of VNTR. Support for this amendment can be found at least at page 2, line 11.

Claim 4 has been amended to clarify that at least one of the adaptor or primers used in step (c) and/or step (d) contains at least one phosphorothioate bond.

Claims 11 and 15 have been further amended to clarify that the subject matter to which the claims are directed. The preambles have been amended to "A mixture of one or more VNTR alleles and their flanking regions." This amendment alleviates any possible confusion as to whether the mixture of alleles are required to be on the same isolated portion of genomic DNA. As amended, it is clear that this is not a requirement of the claim. Support for this amendment can be found throughout the specification and original claims. For example, "A mixture of one or more VNTR alleles and their flanking regions" is the product of claim 1. Claim 12 has been amended such that the preamble matches claim 11 from which it depends.

Claim 14 has been amended wherein to be directed to a composition consisting essentially of one or more copies of a single variable number tandem repeat (VNTR) allele and its flanking regions and an adaptor at each of its 3'-end and its 5'-end, said allele being characteristic of those which manifest a trait of interest. Support for the amendment can be found throughout the specification and original claims. For example, the composition is a product of claim 6.

Claim 21 has been amended to properly include a gerund at the beginning of step (d).

Claim 22 is amended herein to be directed to methods wherein a composition consisting essentially of molecules of nucleic acid containing a polymorphic allele and its flanking sequences representative of those which manifest the trait of interest are incubated under hybridization conditions with a mixture of molecules of nucleic acid which contain polymorphic alleles and their flanking sequences representative and derived from more than one of those which do not manifest the trait of interest. Support for this amendment can be found throughout the specification, *e.g.*, at least at pages 28 and 29.

Claim 25 is amended herein to be directed to a method for diagnosing using a composition consisting essentially of one or more copies of a single variable number tandem repeat (VNTR) allele and its flanking regions and an adaptor at each of its 3'-end and its 5'-end, said allele being characteristic of those which manifest a trait of interest. Support for the amendment can be found throughout the specification and original claims, *e.g.*, see original claim 26.

Claim 26 has been amended to correctly spell "hybridisation."

II. Priority

Applicant is in the process of retrieving a certified copy of the priority document. Upon receiving the certified copy, Applicant plan to submit it to the USPTO by supplemental amendment.

III. Oath or Declaration

A new Declaration identifying the present application by application number and filing date is submitted herewith.

IV. Claim Objections

Claims 1, 11, 14, 15, 17, and 21 have been amended to include the non-abbreviated VNTR.

V. Outstanding Rejections

Claims 1-10, and 26-27 stand rejected under 35 U.S.C. §112 (second paragraph) as being indefinite.

Claims 1-10 and 21 stand rejected under 35 U.S.C. §112 (first paragraph) as containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claims 11-15 stand rejected under 35 U.S.C. §102(b) as being anticipated by Morgante et al. WO 96/17082.

Claims 16, 22-23 and 25 stand rejected under 35 U.S.C. §102(b) over Nelson et al.

Claims 17-20, 22-27 stand further rejected under 35 U.S.C. §103(a) over Nelson et al., as applied to claims 16, 22-23 and 25, and further in view of Grist et al and Aldhous.

VI. Patentability Arguments

A. The Rejections under 35 U.S.C. §112, Second Paragraph, Should be Withdrawn

Claim 1 stands rejected as allegedly indefinite for several reasons. During the discussion of November 21, 2002, the undersigned went through claim 1 with the Examiners step by step pointing to exemplary text and diagrams within the specification corresponding with each step. Examiner Schmidt indicated that she had misunderstood the claim and the explanation clarified the misunderstanding. Applicant summarizes the explanation provided during the discussion below. This explanation uses exemplary embodiments for instructional purposes only and should not be viewed as a limitation of claim 1 to those exemplary embodiments.

Applicant draws the Examiner's attention to pages 14-21 of the specification. Step (a) recites "dividing genomic DNA of the species of interest into fragments." Pages 14 and 15 discuss different methods of achieving step (a) and a diagram of a resulting DNA fragment. Examples, including diagrams, of different ways of achieving step (b) are provided on pages 16 and 17.

The Office Action of May 28, 2002 expressed confusion over the difference of steps (c) and (d) regarding 5' and 3' orientation. As discussed and diagramed on pages 19 and 20, 5' and 3' orientation are determined relative to the VNTR. Using the (AC)_n dinucleotide repeat as an example, the VNTR has repeated ACs from 5' to 3' on one strand and repeated GTs from 5' to 3' on the other strand.

5' -...ACACACACACAC...- 3'
3' -...TGTGTGTGTGTG...- 5'

The VNTR primer of step (c) hybridizes to and primes polymerization to the "left" of the VNTR region as shown in the figure on page 19. The adapter primer allows PCR-like amplification with the VNTR primer to produce an amplicon containing genomic DNA 5' of the VNTR (relative to AC'). The VNTR antisense primer of step (d) hybridizes to and primes polymerization to the "right" of the VNTR region. The adapter primer allows PCR-like amplification with the antisense VNTR primer to produce an amplicon containing genomic DNA 3' of the VNTR (relative to AC'). Diagrams of the resulting fragments from steps (c) and (d) are provided on the bottom of page 20 on the left and right, respectively.

Furthermore, the Office Action of May 28, 2002 stated it was allegedly unclear how the genomic DNA is used as a template. As explained on page 21, one or more amplicons can be used to recreate the full-length alleles together with their flanking sequences. The diagrams on pages 25-27 illustrate exemplary embodiments of step (e). Applicant respectfully submits that claim 1 particularly points out and distinctly claims the subject matter which Applicant regards as the invention. Reconsideration of the definiteness of claim 1 (and dependent claims 2-10 and 26-27) in view of the specification as provided in the explanation above is respectfully requested.

Regarding the specific rejection of claim 9, Applicant submits that pages 36-41 provide an excellent explanation of selecting alleles representative of a trait of interest and those representative of alleles representative of those which do not manifest a trait of interest. Furthermore, the pages describe selecting at least one match and/or mismatch. In light of this explanation, Applicant submits that the metes and bounds of claim 9 is definite. Reconsideration is respectfully requested.

Regarding the specific rejection of claim 2, as discussed above, examples of step (b) are provided in the specification at pages 16 and 17 as (A), (B), and (C). An

exemplary embodiment of claim 2 is provided as Method (A). Reconsideration is respectfully requested.

Regarding the specific rejections of claims 4 and 26, claim 4 has been amended herein to clarify that at least one of the primers or adaptors used in step (c) and /or step (d) contains at least one phosphorothioate bond. Claim 26 has been amended to correctly spell "hybridisation." Reconsideration is respectfully requested.

B. The Rejections under 35 U.S.C. §112, First Paragraph, Should be Withdrawn

The Office Action of May 28, 2002 contends that the Applicant was not in possession of the claimed subject matter at the time of filing. This contention is based on a knowledge of the structure of VNTR alleles and the linkage of specific structures to a trait of interest. However, as the explanation above makes clear, the structure of VNTR alleles and their linkage to a trait of interest are not required to perform the methods of claims 1-10, and 21 or can be determined using the specification as a guide. Indeed, one of the important aspects of the invention is determining the structure of VNTR alleles and their linkage to a trait of interest (see abstract).

The specification is replete with explanation, diagrams, and examples of performing the steps of claims 1-10, and 21. As explained on page 46, the invention is suited to any type of VNTR. Examples of VNTRs are given. Using primers to the VNTR sequence and adapters, one could amplify known or unknown VNTR alleles and their flanking regions without the knowledge of the length of the VNTR or the sequence of the flanking regions. Furthermore, the specification describes how one could determine linkage of a VNTR allele to a trait of interest. Thus, Applicant was in possession of the subject matter of the claims at the time of filing and the specification enables the subject matter of the claims. Applicant

respectfully requests withdrawal of the rejection of claims 1-10, and 21 under 35 U.S.C. §112, first paragraph.

C. The Section 102 Rejection of Claims 11-15 Over Morgante Should be Withdrawn.

Claims 11-15 are amended herein to clarify the subject matter of the claims. As clarified, Morgante does not disclose the subject matter of the claims. A schematic of the method of Morgante is provided in Fig. 11 and the description of the figure (page 18). The method of Morgante fragments the genomic DNA and ligates site specific adaptors to each end. However, because most of the fragments do not contain an SSR, such SSR-containing fragments with adaptors at both ends are only a minor portion within the mixture. Thus, Morgante does not disclose a mixture of one or more VNTR alleles and their flanking regions wherein the mixture **consists essentially of** a representative mixture of alleles of a chosen VNTR sequence and their flanking regions on both sides mixture of discloses a method of cloning and sequencing a chosen simple sequence repeat (claims 11 and 12), a composition **consisting essentially of** one or more copies of a VNTR allele and its flanking regions (claim 14), of a mixture **consisting essentially of** a representative mixture of 3'-flanking regions of a chosen VNTR and a representative mixture of 5'-flanking regions of a chosen VNTR (claim 15). (As a side note, Applicant points the Examiner's attention to an error in Fig. 11 of Morgante. PCR using the lsfp-1 primer and the AD_A primer would not yield a fragment having adaptor sequence at both ends as depicted in the figure (third construct down). Rather, the product would resemble the fourth construct down.). Applicant respectfully requests reconsideration of the novelty of claims 11-15 in view of Morgante.

D. The Rejections under 35 U.S.C. § 102(b) Over Nelson Should be Withdrawn

The rejection of claims 16, 22-23 and 25 under 35 U.S.C. §102(b) over Nelson et al. should be withdrawn. Regarding claim 16, the nucleic acids being treated in Nelson are digested genomic DNA, which do not consist essentially of a mixture of polymorphic alleles representative of those which manifest a trait of interest. Indeed, any VNTR allele would be an extremely minor portion of the fragmented genomic DNA. Thus, Nelson does not anticipate claim 16.

Regarding claims 22-23, and 25, Nelson discloses comparing the genomic DNA of two individuals (see figure 1). At best, the method of Nelson would include a step wherein the genomic DNA from an **individual** having a trait of interest is hybridized to the genomic DNA of an **individual** not having the trait of interest. Nelson does not disclose incubating together under hybridization conditions: a composition consisting essentially of nucleic acid containing a polymorphic allele and its flanking sequences representative of those which manifest a trait of interest; and a mixture of molecules of nucleic acid which contain polymorphic alleles and their flanking sequences representative **and derived from more than one** of those which do not manifest the trait of interest, as claim 22 is directed to as amended herein.

In light of the above arguments, Applicant respectfully requests reconsideration of the novelty to claims 16, 22-23, and 25.

E. The Rejections under 35 U.S.C. § 103 Should be Withdrawn

The rejection of claims 17-20, 22-27 rejected under 35 U.S.C. §103(a) over Nelson et al., as applied to claims 16, 22-23 and 25, and further in view of Grist et al and Aldhous, should be withdrawn. Claims 17-20 and 26 are dependent on claim 16. As discussed above, the nucleic acids being treated in Nelson are digested genomic DNA, which

do not consist essentially of a mixture of polymorphic alleles representative of those which manifest a trait of interest. The cited secondary art does not suggest substituting the genomic DNA of Nelson with nucleic acids consisting essentially of a mixture of polymorphic alleles. Thus, claims 17-20 and 26 are nonobvious in light of the cited art.

Furthermore, the cited art does not disclose or suggest the subject matter of claims 22-27. Regarding claims 22-24, the secondary art does not suggest substituting the genomic DNA of Nelson with a composition **consisting essentially of** nucleic acid containing a polymorphic allele and its flanking sequences representative of those which manifest the trait of interest and a mixture of molecules of nucleic acid which contain polymorphic alleles and their flanking sequences representative **and derived from more than one** of those which do not manifest the trait of interest.

Claim 26, as amended herein, is directed to a method for diagnosing a trait of interest comprising the step of identifying an allele which is linked to a trait of interest according to the method of claim 22, wherein said molecules of nucleic acid are contacted with a composition consisting essentially of one or more copies of a single VNTR allele and its flanking regions and an adaptor at each of its 3'-end and its 5'-end, said allele being characteristic of those which manifest a trait of interest. As discussed above, neither Nelson nor the cited secondary references disclose or suggest the method of claim 22, moreover, wherein the molecules of nucleic acid are contacted with a composition consisting essentially of one or more copies of a single VNTR allele and its flanking regions and an adaptor at each of its 3'-end and its 5'-end.

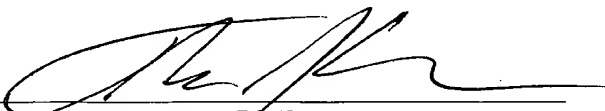
CONCLUSION

For all of the foregoing reasons, the rejections should now be withdrawn and an early notice of all pending claims is respectfully solicited. Should the Examiner wish to discuss any issues of form or substance in order to expedite allowance of the pending application, she is encouraged to contact the undersigned attorney at the number indicated below.

Respectfully submitted,

MARSHALL, GERSTEIN & BORUN

By:



Thomas J. Wrona, Ph.D.
Reg. No. 44,410
6300 Sears Tower
233 South Wacker Drive
Chicago, Illinois 60606-6357
(312) 474-6300

November 27, 2002

APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 1, 4, 11, 12, 14,15, 17, 21, 22, 25, and 26 have been amended as follows:

1. [Thrice Amended] A method of making a mixture of variable number tandem repeat (VNTR) alleles and their flanking regions of the genomic DNA of one or more members of a species of interest, which method comprises the steps of:
 - a) dividing genomic DNA of the species of interest into fragments,
 - b) ligating to each end of each fragment an adapter thereby forming a mixture of adaptor-terminated fragments in which each 3'-end is blocked to prevent enzymatic chain extension,
 - c) contacting a portion of the mixture of adaptor-terminated fragments with an adaptor primer and a VNTR primer wherein said portion of the mixture of adaptor terminated fragments serves as a template to create a mixture of 5'-flanking VNTR amplimers;
 - d) contacting a portion of the mixture of adaptor-terminated fragments with an adaptor primer and a VNTR antisense primer wherein said portion of the mixture of adaptor-terminated fragments serves as template to create a mixture of 3'-flanking VNTR amplimers,
 - e) and producing a desired mixture of VNTR alleles and their flanking regions by contacting genomic DNA of the one or more members of the species of interest with the mixture of 5'-flanking VNTR amplimers and/or the mixture of 3'-flanking VNTR amplimers as primers wherein said genomic DNA of the one or more members of the species of interest is used as template.

4. [Amended] The method of claim 1, wherein in step c) and/or d) [the] at least one adaptor or primer used contains at least one phosphorothioate bond.
11. [Twice Amended] A mixture of one or more VNTR alleles and their flanking regions [An isolated portion of genomic DNA of one or more members of a species of interest], said mixture [portion] consisting essentially of a representative mixture of alleles of a chosen variable number tandem repeat (VNTR) sequence and their flanking regions on both sides, wherein each member of the representative mixture of alleles has an adaptor at each of its 3'-end and its 5'-end [and which is representative of that member or members].
12. [Amended] The mixture of one or more VNTR alleles and their flanking regions of [The isolated portion as claimed in] claim 11, wherein the mixture of alleles is representative of those which manifest a trait of interest.
13. Cancelled.
14. [Twice Amended] A composition [An isolated portion of genomic DNA of one or more members of a species of interest, said portion] consisting essentially of one or more copies of a single variable number tandem repeat (VNTR) allele and its flanking regions and an adaptor at each of its 3'-end and its 5'-end, said allele being characteristic of those which manifest a trait of interest.
15. [Twice Amended] A mixture of VNTR flanking sequences, said mixture [An isolated portion of genomic DNA of a species of interest, said portion] consisting essentially

of a representative mixture of 3'-flanking regions of a chosen variable number tandem repeat (VNTR) sequence, each member of the mixture carrying an adaptor at its 3'-end, and a representative mixture of 5'-flanking regions of a chosen VNTR sequence, each member of the mixture carrying the same adaptor at its 5'-end.

17. [Once Amended] The method of claim 16, wherein the mixture of polymorphic alleles is a mixture of alleles of a chosen variable number tandem repeat (VNTR) sequence and their flanking regions.
21. [Thrice Amended] A method of making a mixture of amplimers which method comprises the steps of:
 - a) dividing genomic DNA of one or more members of a species of interest into fragments,
 - b) ligating to each end of each fragment an adaptor thereby forming a mixture of adaptor-terminated fragments in which each 3'-end is blocked to prevent enzymatic chain extension, and
 - c) contacting a portion of the mixture of adaptor-terminated fragments with an adaptor primer and a variable number tandem repeat (VNTR) primer wherein said portion of the mixture of adaptor-terminated fragments serves as a template to create a mixture of 5'-flanking VNTR amplimers, and/or
 - d) contacting a portion of the mixture of adaptor-terminated fragments with an adaptor primer and a VNTR antisense primer wherein said portion of the mixture of adaptor-terminated fragments serves as a template to create a mixture of 3'-flanking VNTR amplimers

22. [Twice Amended] A method of identifying an allele which is linked to a trait of interest, which method comprises incubating together under hybridisation conditions: a composition consisting essentially of [at least one] molecules of nucleic acid containing a polymorphic allele and its flanking sequences representative of those which manifest the trait of interest; and a mixture of molecules of nucleic acid which contain polymorphic alleles and their flanking sequences representative and derived from more than one of [alleles] those which do not manifest the trait of interest; and selecting at least one match and/or at least one mis-match to provide at least one allele or fragment thereof which is linked to the trait of interest.
25. [Thrice Amended] A method for diagnosing a trait of interest comprising the step of identifying an allele which is linked to a trait of interest according to the method of claim 22, wherein said molecules of nucleic acid are contacted with [an isolate portion of genomic DNA of one or more members of a species of interest, said portion] a composition consisting essentially of one or more copies of a single VNTR allele, and its flanking regions and an adaptor at each of its 3'-end and its 5'-end, said allele being characteristic of those which manifest a trait of interest.
26. [Amended] The method of claim 1 or claim 16, wherein the VNTR allele and its flanking regions, or the mixture of VNTR alleles and their flanking regions, is analysed by being applied under [hybridisation] hybridisation conditions to an array of immobilised VNTR alleles and/or their flanking regions.

APPENDIX B

Pending claims in the application:

1. A method of making a mixture of variable number tandem repeat (VNTR) alleles and their flanking regions of the genomic DNA of one or more members of a species of interest, which method comprises the steps of:
 - a) dividing genomic DNA of the species of interest into fragments,
 - b) ligating to each end of each fragment an adapter thereby forming a mixture of adaptor-terminated fragments in which each 3'-end is blocked to prevent enzymatic chain extension,
 - c) contacting a portion of the mixture of adaptor-terminated fragments with an adaptor primer and a VNTR primer wherein said portion of the mixture of adaptor terminated fragments serves as a template to create a mixture of 5'-flanking VNTR amplimers;
 - d) contacting a portion of the mixture of adaptor-terminated fragments with an adaptor primer and a VNTR antisense primer wherein said portion of the mixture of adaptor-terminated fragments serves as template to create a mixture of 3'-flanking VNTR amplimers,
 - e) and producing a desired mixture of VNTR alleles and their flanking regions by contacting genomic DNA of the one or more members of the species of interest with the mixture of 5'-flanking VNTR amplimers and/or the mixture of 3'-flanking VNTR amplimers as primers wherein said genomic DNA of the one or more members of the species of interest is used as template.
2. The method of claim 1, wherein step b) is performed by terminating each end of each fragment to prevent enzymatic chain extension, and ligating each 5'-end of

each fragment to an adaptor, thereby forming a mixture of adaptor terminated fragments.

3. The method of claim 1, wherein in step c) the VNTR repeat sequences are removed from the 5'-flanking VNTR amplimers, and in step d) the VNTR repeat sequences are removed from the 3'-flanking VNTR amplimers.
4. The method of claim 1, wherein in step c) and/or d) at least one adaptor or primer used contains at least one phosphorothioate bond.
5. The method of claim 1, wherein step e) is performed using as primers, successively or together, both the mixture of 5'-flanking VNTR amplimers and the mixture of 3'-flanking VNTR amplimers.
6. The method of claim 1, wherein there is used in step e) genomic DNA of one or more members of the species of interest which manifest a trait of interest, whereby the resulting mixture of VNTR alleles and their flanking sequences is representative of those which manifest the trait of interest.
7. The method of claim 6 wherein in a step f) the strands of the mixture of VNTR alleles and their flanking regions are separated and then re-annealed and any mismatches are separated and discarded.
8. The method of claim 7, wherein step f) is repeated to recover a single VNTR allele and its flanking regions.

9. The method of claim 6, wherein at least one VNTR allele and its flanking sequences representative of those which manifest the trait of interest, is hybridised with a mixture of VNTR alleles and their flanking sequences representative of alleles which do not manifest the trait of interest, and at least one match and/or at least one mis-match is selected to provide at least one VNTR allele or fragment thereof which is characteristic of the trait of interest.
10. The method of claim 9, wherein the at least one VNTR allele and its flanking sequences representative of those which manifest the trait of interest, is provided with 3'-overlapping ends.
11. A mixture of one or more VNTR alleles and their flanking regions, said mixture consisting essentially of a representative mixture of alleles of a chosen variable number tandem repeat (VNTR) sequence and their flanking regions on both sides, wherein each member of the representative mixture of alleles has an adaptor at each of its 3'-end and its 5'-end.
12. The mixture of one or more VNTR alleles and their flanking regions of claim 11, wherein the mixture of alleles is representative of those which manifest a trait of interest.
14. A composition consisting essentially of one or more copies of a single variable number tandem repeat (VNTR) allele and its flanking regions and an adaptor at each

of its 3'-end and its 5'-end, said allele being characteristic of those which manifest a trait of interest.

15. A mixture of VNTR flanking sequences, said mixture consisting essentially of a representative mixture of 3'-flanking regions of a chosen variable number tandem repeat (VNTR) sequence, each member of the mixture carrying an adaptor at its 3'-end, and a representative mixture of 5'-flanking regions of a chosen VNTR sequence, each member of the mixture carrying the same adaptor at its 5'-end.
16. A method of treating nucleic acids which consist essentially of a mixture of polymorphic alleles, the mixture being representative of those which manifest a trait of interest, which method comprises separating and then re-annealing strands of the mixture, and separating and discarding any mis-matches.
17. The method of claim 16, wherein the mixture of polymorphic alleles is a mixture of alleles of a chosen (VNTR) sequence and their flanking regions.
18. The method of claim 17, wherein the method is repeated to recover a single VNTR allele and its flanking regions.
19. The method of claim 17, wherein at least one VNTR allele and its flanking sequence representative of alleles which manifest the trait of interest, is hybridised with a mixture of VNTR alleles and their flanking sequences representative of those which do not manifest the trait of interest, and at least one match and/or at least one

mis-match is selected to provide at least one VNTR allele or fragment thereof which is characteristic of the trait of interest.

20. The method of claim 19, wherein the at least one VNTR allele and its flanking sequence representative of alleles which manifest the trait of interest, is provided with overlapping ends.

21. A method of making a mixture of amplimers which method comprises the steps of:

- a) dividing genomic DNA of one or more members of a species of interest into fragments,
- b) ligating to each end of each fragment an adaptor thereby forming a mixture of adaptor-terminated fragments in which each 3'-end is blocked to prevent enzymatic chain extension, and
- c) contacting a portion of the mixture of adaptor-terminated fragments with an adaptor primer and a variable number tandem repeat (VNTR) primer wherein said portion of the mixture of adaptor-terminated fragments serves as a template to create a mixture of 5'-flanking VNTR amplimers, and/or
- d) contacting a portion of the mixture of adaptor-terminated fragments with an adaptor primer and a VNTR antisense primer wherein said portion of the mixture of adaptor-terminated fragments serves as a template to create a mixture of 3'-flanking VNTR amplimers

22. A method of identifying an allele which is linked to a trait of interest, which method comprises incubating together under hybridisation conditions: a composition

consisting essentially of molecules of nucleic acid containing a polymorphic allele and its flanking sequences representative of those which manifest the trait of interest; and a mixture of molecules of nucleic acid which contain polymorphic alleles and their flanking sequences representative and derived from more than one of those which do not manifest the trait of interest; and selecting at least one match and/or at least one mis-match to provide at least one allele or fragment thereof which is linked to the trait of interest.

23. The method of claim 22, wherein the alleles are VNTR alleles.
24. The method of claim 22, wherein the at least one allele and its flanking sequences representative of alleles which manifest the trait of interest, is provided with 3'-overlapping ends.
25. A method for diagnosing a trait of interest comprising the step of identifying an allele which is linked to a trait of interest according to the method of claim 22, wherein said molecules of nucleic acid are contacted with a composition consisting essentially of one or more copies of a single VNTR allele and its flanking regions and an adaptor at each of its 3'-end and its 5'-end, said allele being characteristic of those which manifest a trait of interest.
26. The method of claim 1 or claim 16, wherein the VNTR allele and its flanking regions, or the mixture of VNTR alleles and their flanking regions, is analysed by being applied under hybridisation conditions to an array of immobilised VNTR alleles and/or their flanking regions.

27. A kit comprising protocols and reagents for performing the method of claim 1 or claim 16 or claim 24.